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*Published in:*  
Social Science & Medicine

*Publication date:*  
1999

*Document Version*  
Publisher's PDF, also known as Version of record

[Link to publication in Tilburg University Research Portal](#)

*Citation for published version (APA):*  
Eugster, A., & Vingerhoets, A. J. J. M. (1999). Psychological aspects of in vitro fertilization: a review. *Social Science & Medicine*, 48(5), 575-589.

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Social Science & Medicine 48 (1999) 575–589

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# Psychological aspects of in vitro fertilization: a review

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## Abstract

This paper reviews psychological research within the context of in vitro fertilization (IVF). The focus will be on psychological reactions before entering an IVF-procedure, during an IVF-treatment, and after both unsuccessful and successful IVF. The effects of psychosocial factors on the treatment outcome after IVF and interventions on conception rates will also be discussed.

Undergoing an IVF-treatment is an emotional and physical burden, for both the woman and her partner. Research results suggest that couples entering an IVF-treatment program are, in general, psychologically well adjusted. Concerning reactions during the treatment, both women and men experience waiting for the outcome of the IVF-treatment and an unsuccessful IVF, as most stressful. Common reactions during IVF are anxiety and depression, while after an unsuccessful IVF, feelings of sadness, depression and anger prevail. After a successful IVF-treatment, IVF-parents experience more stress during pregnancy than 'normal fertile' parents. Mothers with children conceived by IVF express a higher quality of parent-child relationship than mothers with a naturally conceived child.

Research further suggests that psychosocial factors, like ineffective coping strategies, anxiety and/or depression are associated with a lower pregnancy rate following IVF-procedures. In addition, support has been found suggesting that stress reduction through relaxation training or behavioral treatment improves conception rates. © 1999 Elsevier Science Ltd. All rights reserved.

*Keywords:* In vitro fertilization; Psychological reactions; Effect of psychosocial factors on treatment outcome

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## 1. Introduction

Over the last few years, impressive progress has been made in the development of medical technological interventions for couples with fertility problems. Depending on the precise nature of the fertility problem, various reproductive technologies are available to help couples achieve a pregnancy. This includes in vitro fertilization (IVF), artificial insemination with the semen of a donor (AID), artificial insemination with the semen of the husband (AIH) and, recently, intracytoplasmic sperm injection (ICSI). Although the reproductive treatments are impressive from a technical

point of view, they nevertheless can be a source of tension for the couples involved. The interventions contain a number of stressful aspects, such as the daily injections, blood samples, ultra-sound scan and a sperm sample from masturbation.

In this article, the literature on the role of psychological reactions to and consequences of in vitro fertilization will be summarized. This review will briefly describe the incidence of infertility and the procedure of IVF. Its main focus will be on psychological issues within the context of in vitro fertilization (IVF), including the psychological states before entering, during and after the IVF-treatment, coping strategies and the effect of psychosocial factors on the treatment outcome after IVF. In addition, the effect of psychological interventions on conception rates will be discussed.

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## 2. Incidence of infertility

Infertility is defined as “the inability of a couple to achieve conception or to bring a pregnancy to term after a year or more of regular, unprotected intercourse” (WHO, 1992). Although having children is taken for granted, not achieving a pregnancy is a common occurrence. According to the WHO (1992), approximately 8–10% of couples worldwide experience some form of infertility problem, with wide differences from region to region. Approximately 10–12% of American couples of reproductive age (Leiblum, 1997) and 14% of Dutch couples (van Balen et al., 1995) who wish to have a child and regularly have unprotected sexual contact, experience difficulties in conceiving. In the Netherlands, the situation is as follows; approximately one out of 10 Dutch couples (Gaasbeek and Leerentveld, 1993; van Balen et al., 1995) who do not conceive after one year consider it a problem and seek professional help. Two thirds of them are referred to a specialist (van Balen et al., 1995). Roughly speaking, of the Dutch couples who pursue pregnancy, 50% achieve their goal after six months, 85–90% after 12 months and 95% after 24 months, partly depending on the woman's age (Gaasbeek and Leerentveld, 1993). The chance of not getting pregnant within one year is 10% for women between the age of 20 and 28 and 25% for 35 year-old women (van Balen et al., 1995).

Infertility is not exclusively a female problem. Infertility can be attributed to the female, the male, or to both the male and female. There are also couples in which the cause of the fertility problem remains unexplained.

## 3. In vitro fertilization

### 3.1. Application

IVF is applied to many forms of infertility, but the criteria differ per center. Initially, the IVF-treatment was applied only to women with blocked ovaries. Nowadays, other fertility problems are also treated with IVF, such as infertility resulting from endometriosis, woman's antibodies against sperm, bad sperm quality or unexplained infertility. The latter means that the woman can not get pregnant, yet there is no medical explanation for this. (van Hall, 1988; DES-Nieuws, 1993; Gaasbeek and Leerentveld, 1993).

### 3.2. Procedure

The essence of IVF is that processes which normally take place in the ovary, now take place in the laboratory. The treatment consists of the following four phases: (1) hormone stimulation (when it concerns a

stimulated cycle): the ovaries are stimulated with the help of medication (pills or injections), (2) oocyte retrieval: the female germ cells are retrieved, just before the follicles pop. Because this procedure can be painful, the woman is administered a calming medication in advance, (3) fertilization: oocytes are inseminated with prepared semen under laboratory conditions (McShane, 1997), after which one has to wait to find out whether or not embryos are formed. The fertilized oocytes stay two till four days in the ‘test-tube’; (4) embryo transfer: the embryos are transferred through a little hose through the cervix into the uterus. Consequently, one has to wait to see whether or not the embryos become implanted in the wall of the uterus. This appears to be the most critical phase (Gaasbeek and Leerentveld, 1993).

The chance of success is larger when more embryos are transferred and further depends on personal factors, for instance, age (Gaasbeek and Leerentveld, 1993; McShane, 1997), smoking (Gaasbeek and Leerentveld, 1993) and the experience of the clinic in carrying out the procedure (DES-Nieuws, 1993; Gaasbeek and Leerentveld, 1993) and varies between 10 and 20% (DES-Nieuws, 1993; Leiblum, 1997). On average, the probability of a pregnancy after three treatments is 40 till 45% (Gaasbeek and Leerentveld, 1993).

### 3.3. Side effects and possible risks of IVF

Applying IVF also includes the risk of possible side effects. The most important side effect is an increased chance of a multiple birth pregnancy (DES-Nieuws, 1993; Gaasbeek and Leerentveld, 1993; Leiblum, 1997). A successful pregnancy becomes more probable when more embryos are transferred, but this at the same time increases the chance of a multiple birth pregnancy. About 25% of all IVF-pregnancies are multiple birth pregnancies (DES-Nieuws, 1993; Leiblum, 1997). When a pregnancy occurs, in 20–25% of the cases it concerns a twin and in 5% triplets (Gaasbeek and Leerentveld, 1993). Today the IVF-centers in the Netherlands agree that, in general, no more than two or three embryos should be transferred (te Velde and Beets, 1994).

As the risk of premature birth delivery increases with a multiple birth pregnancy, the inherent risk that the babies will die or have a handicap in the case of survival, is much higher than in a normal pregnancy (DES-Nieuws, 1993; Gaasbeek and Leerentveld, 1993; Leiblum, 1997). The mortality rate among IVF multiple births is about five times higher than among IVF single births (Berkhout, 1995). Leiblum (1997) discussed a French study, which examined, among other things, the incidence of prematurity associated with the use of IVF in France between 1986 and 1990. They

found that the preterm birth rate, 29.3% and the low birth weight rate, 36.3%, were elevated when compared with natural conception (Fivnat and Institut National, 1995).

Another important possible side effect of IVF is the ovarian hyperstimulation syndrome (OHS) or overstimulation (DES-Nieuws, 1993; Gaasbeek and Leerentveld, 1993; Leiblum, 1997), which can occur when the ovaries are reacting too strongly to the hormones. This leads to maturation of too many egg-cells and enlargement of the ovaries. In serious cases, the ovaries are full of follicles filled with fluid, which may result in serious complications, such as thrombosis, embolism and even death. The chance of overstimulation is estimated at 0.5–4% (DES-Nieuws, 1993; Gaasbeek and Leerentveld, 1993). In addition, administering Clomiphene, HMG, HCG or LHRH-analogous can cause all sorts of side effects. Clomiphene influences the hormone production, including the follicle stimulating hormone (FSH) and thereby stimulates the maturation of the female germ cell (Gaasbeek and Leerentveld, 1993). Although several potential side effects of using Clomiphene have been suggested, (Gaasbeek and Leerentveld, 1993; McShane, 1997), these seem to occur only rarely in practice. Amongst them are hot flushes, nausea, tiredness, weight increase, sensitive breasts, but also depression and anxiety. LHRH-analogous can also induce hot flushes and headaches. Indeed, all hormones can negatively affect emotional stability (Gaasbeek and Leerentveld, 1993).

At the moment, little is known about the biological and psychological long-term effects of IVF and in particular the application of the hormones on mother and child (Gaasbeek and Leerentveld, 1993). van Hall (1988) does not rule out that women who repeatedly underwent hyperstimulation and puncture of the ovaries, will have an increased risk of developing serious diseases, e.g. ovarian cancer, in the long term. Meanwhile, there are indeed epidemiological indications that stimulating the ovaries with gonadotropins increases the risks of ovarian cancer (Whittemore et al., 1992). Therefore, it is necessary to follow IVF-children and their mothers over a longer period (van Hall, 1988). Only future long-term longitudinal study can reveal to what extent IVF has damaging consequences for the anatomy and functioning of reproductive organs of both mother and child.

#### 4. Psychological reactions before and during IVF

Undergoing an IVF-treatment is an emotional and physical burden, for both the woman and her partner. Aspects like the hormone treatments, the sometimes daily returning blood tests, daily ultra sound scans, masturbating, waiting until the female germ cells are

maturing well, the puncture, waiting if the fertilization takes place, the transfer and waiting if one gets pregnant can interfere with other matters in a couple's life (Gaasbeek and Leerentveld, 1993). The different stages of the IVF-procedure can influence the psychosocial functioning of the man and the woman negatively.

##### 4.1. Psychological status before entering an IVF-treatment program

Research results suggest that couples entering an IVF-program are, in general, psychologically well adjusted (Hearn et al., 1987; Shaw et al., 1988; Newton et al., 1990; Edelmann et al., 1994). In a study of Edelmann et al. (1994) among 152 couples who did not have previous experience with IVF, a coping questionnaire and standardized psychological instruments measuring personality, general health, self-esteem, anxiety and mood state were administered preceding their first IVF-treatment. The results of the couples showed little deviation from the normative data on the standardized measures. Although the scores on state and trait anxiety for females were slightly elevated relative to normative data on working adults (Edelmann et al., 1994), scores on the General Health Questionnaire (GHQ; Goldberg, 1978) were even slightly lower than the normative data, while scores concerning self-esteem, mood and personality resembled normative data. The authors therefore concluded that couples presenting for IVF are, in general, psychologically well adjusted, irrespective of their fertility history and duration of infertility. Because the results were opposite to their expectations, Edelmann et al. (1994), like Callan and Hennessey (1988), sought the explanation for their findings partly in a self-selection effect. This means that only psychologically well adjusted couples will seek medical help in their efforts to get pregnant and choose to confront the emotional demands of an IVF-treatment. In couples who are not psychologically adjusted, the relationship may be too vulnerable to restrain the extra burden of more infertility investigations. Another explanation might be that because these couples have experienced years of infertility, they may have developed ways of handling the stress associated with it, particularly well (Freeman et al., 1985).

In a study of Hearn et al. (1987) among 300 couples entering an IVF-treatment program, it was also found that couples did not differ from normative data with respect to overall life satisfaction, overall well-being and depression. Women did not differ from normative data on state and trait anxiety, whereas the men were even significantly less anxious than the norm. Interpretation of the findings was limited by several factors. The most important limitation was that respondents evidenced some bias toward socially acceptable responses. Newton et al. (1990) studied the

emotional status of couples entering an IVF-program (947 women and 899 male partners). In comparison to their male partners, women experienced significantly higher levels of state anxiety, trait anxiety and depression. However, group means were in the clinically normal range. Shaw et al. (1988) in their study with 118 couples on the waiting list for IVF also found little evidence that such couples show emotional and/or marital problems. This in contrast to previous studies (for example Kraft et al., 1980; Bell, 1981). Shaw et al. (1988) explained the inconsistent results in whether or not the results were compared with a norm. Edelmann et al. (1994), Hearn et al. (1987), Newton et al. (1990) and Shaw et al. (1988) compared the results of couples with fertility problems with other couples or with a norm, whereas previous studies (Kraft et al., 1980; Bell, 1981) did not.

In a study among 86 IVF women, Visser et al. (1994) found that, prior to their first IVF, women scored higher on state anxiety than the norm group, but did not suffer more from general complaints than the normal population.

In a longitudinal study by Slade et al. (1997) among 144 couples undergoing IVF, it has been demonstrated that at intake, IVF women scored significantly higher on state anxiety, trait anxiety and depression than their partners. They also scored significantly lower on self-esteem than their partners, but the scores fell in the clinically normal range. For women, both state and trait anxiety scores were significantly above the normative data of working adults, while men scored below it. The IVF-women did not significantly differ from norms on depression, while men scored below the expected range. Concerning the quality of the marital relationship, women were less satisfied with their relationships and had lower total scores than their partners. The overall level of marital adjustment of women was also lower than the norms for married couples. Compared to normative data, both men and women had significantly lower scores on consensus and higher scores on cohesion. However, the norms used were derived from combined males and females scores, whereas in this study the scores were recorded separately. Although in this study some deviation from normative data was reported, the women's state and trait anxiety scores were similar to the data presented by Edelmann et al. (1994), suggesting that couples entering an IVF-program are, in general, well adjusted.

According to Beaurepaire et al. (1994), the reason why women who just start with the IVF-procedures display relatively normal levels of depression is because depression results from actual loss. When the initial shock of diagnosis is behind them, women start with an IVF procedure with unrealistically high expectations of success on the treatment (Baram et al., 1988; Beaurepaire et al., 1994). These high expectations tem-

porarily temper their feelings of loss. When however after repeated IVF-procedures no pregnancy occurs, the loss will be more current and more concrete because the women then realize that they will probably never bear a child. This makes them and especially those who use less effective coping strategies (Demyttenaere et al., 1991), more vulnerable to developing clinical depression.

Both partners tend to be overly optimistic and have unrealistically high expectations about the likelihood of a successful pregnancy after an IVF-treatment (Collins et al., 1992; Visser et al., 1994).

#### 4.2. Stress during IVF

Couples tend to rate the IVF procedure as moderately stressful (Leiblum et al., 1987; Baram et al., 1988). One-third of the participants evaluate IVF as very stressful (Leiblum et al., 1987). The most stressful aspects for both men and women are waiting to hear the outcome of embryo transfer (Connolly et al., 1993), waiting for the outcome of IVF (Baram et al., 1988; Dudok de Wit, 1992; Connolly et al., 1993; Laffont and Edelmann, 1994) and an unsuccessful IVF (Baram et al., 1988; Laffont and Edelmann, 1994).

In the retrospective study by Dudok de Wit (1992), 41 couples (10 pregnant, 31 not pregnant) who no longer had IVF treatments (stopped 3–12 months earlier), were asked to what extent they had experienced the IVF-treatments as demanding. At each phase, the self-reported tension increased, decreased during embryo-transfer and again increased strongly during the period of waiting to find out whether the embryos had become implanted. It was striking that the phases in which there was no actual contact with the ward were experienced as rather stressful. When there was no actual contact with the hospital, couples scored low on support from the hospital. No significant differences between partners were found concerning experienced burden and experienced support from the hospital. Also, no significant differences were found between the pregnant and the nonpregnant group.

In a study by van Balen et al. (1996), the burden of infertility treatments was investigated among IVF patients who got their first child through IVF and other formerly infertile parents (pregnancy without IVF). Results showed that both the IVF parents and the other, formerly infertile, parents experienced the fertility investigations and treatments more as a psychological than as a physical burden. Judged afterwards, however, both men and women in this successful group found the treatments worthwhile. But as indicated by the authors, this might not be the case for couples with an unsuccessful IVF.

In a study by Laffont and Edelmann (1994), gender differences in the impact of IVF, stressful aspects of

treatment and reaction to a failed IVF attempt were evaluated. The participants, 117 women and 101 men, had been through at least one IVF attempt. Data were collected at one point in time. During hormone stimulation, women had to complete the questionnaire at home, independently of their partners. Data of the men were collected prior to sperm collection. Both men and women rated waiting for the pregnancy result and a negative pregnancy result as most stressful, women significantly more than men. Women further reported that IVF is more disruptive to their work and leisure activity than it is for men. The women also rated the travel involved in treatment as more stressful than the men. According to the investigators, the observed gender differences are consistent with the women's greater personal involvement in IVF. It was also suggested that the observed gender differences could not be interpreted as a more general reflection of gender differences in stress responses, because scores on the General Health Questionnaire (GHQ; Goldberg, 1978), a screening measure for psychiatric morbidity, were higher for women than men in relation to available comparable data for fertile single and married women and men. The question is to what extent the observed gender differences were due to the fact that the women were assessed during their hormone stimulation. It is commonly known that the hormones used to stimulate the ovarians can affect mood negatively. Thus it may not be excluded that the results in this study are, at least partly, a reflection of the effects of hormone stimulation instead of resulting from the stressfulness of aspects of an IVF-treatment.

In a study of Boivin and Takefman (1996), 20 women completed a daily symptom checklist for one complete menstrual cycle and one complete IVF cycle. Average scores, representing three phases of the menstrual cycle or IVF cycle (follicular/stimulation, ovulatory/retrieval-transfer and luteal/waiting period), showed that during the phase of the retrieval-transfer and the waiting period more stress was reported than during the ovulatory and luteal phase in the no-treatment cycle.

In interviews before an IVF treatment, the causes of distress mentioned by couples were hopes and anxiety directly related to the IVF-procedure, their long infertility histories, fear for the oocyte retrieval, uncertainty about the possible effects of possible negative results on the marital relationships and unidentified anxiety about getting pregnant (Brandt and Zech, 1991).

#### 4.3. Anxiety and depression during IVF

The results of the cross-sectional study by Beaurepaire et al. (1994) suggest that both men and women experience anxiety during an IVF-treatment, independent of the stage of the procedure (first time or

repeated cycle). State anxiety can be considered as an indicator of the acute ineffectiveness of the used coping strategies, while trait anxiety (like depression) might be regarded as an indicator of the chronic ineffectiveness of one's coping strategies (Demyttenaere et al., 1991). In this context, state anxiety can be seen as an acute effect of the treatment procedure, for instance because of the uncertainty about the treatment outcome or taking medication, while trait anxiety reflects more a chronic state as a result of the experience of infertility or previous treatment procedures.

During the IVF-procedure, women report more anxiety than their partners (Beaurepaire et al., 1994; Laffont and Edelmann, 1994). This may reflect not only the generally higher anxiety levels of women, but also the greater impact of the treatment on women (Shaw et al., 1988). Women are physically more involved in the IVF-treatment, explaining their greater treatment stress than their partner (Beaurepaire et al., 1994). There is substantial evidence that the IVF-treatment involves many negative psychological aspects for women. On the other hand, the negative impact of the different aspects of the IVF-treatment on men also should not be underestimated (Beaurepaire et al., 1994). Men may, for instance, experience anxiety when they have to produce semen in the hospital.

Reading et al. (1989a) studied psychological reactions in 37 women over the course of IVF. The women were assessed at the beginning of the treatment, at day 8 (follicular phase) and following treatment outcome. Results on the GHQ (Goldberg, 1972) revealed that at the beginning of the treatment, about 20% of the IVF women had clinical signs of anxiety and depression. Concerning scores on the GHQ, the researchers did not control for numbers of treatments the women underwent. Scores on a measure of stress increased significantly over time. During the follicular phase and following the treatment, scores on stress were significantly higher for the IVF women, compared with the comparison group (10 women, not pregnant or trying to get pregnant) and normative data. Concerning mood, scores on anger and confusion increased significantly over time. During the follicular phase, IVF women scored lower on vigor and higher on fatigue than the comparison group. Following treatment outcome, IVF women had significantly higher scores on tension, depression, fatigue and confusion and lower scores on vigor than the comparison group. However, compared with normative data, scores on mood, with exception of depression, remained low over time (Reading et al., 1989a). No significant differences were found between women who underwent their first cycle and women who underwent a repeated cycle. Results of this study have to be interpreted cautiously, since the sample was small. Of the 37 participants, 11 were canceled before oocyte retrieval.

One-hundred and thirteen women with a mechanical or an unexplained infertility were studied during an IVF-treatment by Merari et al. (1992). This prospective study was designed to investigate the psychological and hormonal changes at three critical points during IVF: (1) shortly before the oocyte retrieval, (2) in the morning of the day of the embryo transfer and (3) in the morning of the day when blood samples were taken for pregnancy tests. Measurements before the onset of the hormone treatment provided baseline measures. Results showed that women in all phases were significantly higher on trait and state anxiety than the population norm. Also, depression was significantly higher than the population norm during all phases, except during embryo transfer. However, these investigators failed to control for number of IVF-treatments, which ranged from 0 to 9.

In order to investigate the efficacy of a nondirective counselling intervention on the psychological state of the patients, 152 couples undergoing their first IVF treatment were randomly assigned to either a control group or an experimental group. In the control condition information about the treatment program was provided, whereas the intervention group received the same information plus three sessions of counselling on three occasions: (1) on their first visit to the clinic (2) just before commencement of the treatment and (3) immediately after the medical follow-up appointment (Connolly et al., 1993). Counselling did not seem to have any effect on the psychological state. No differences were found between the treatment and the control groups on state anxiety and scores on the GHQ (Goldberg, 1978). For both sexes, state anxiety decreased while GHQ scores increased during the treatment. For the female participants, there was a significant shift towards depression at the end of the treatment cycle. However, the authors did not compare these scores with a population norm, preventing any definitive conclusions about the extent to which these couples experienced anxiety, depression or psychiatric morbidity during the treatment. Several explanations were given by the authors why in this study counselling was of little importance. Because this goes beyond the scope of this article, we refer to Connolly et al. (1993).

In a biochemical and questionnaire-based assessment of stress in infertile women, Harlow et al. (1996) measured changes in serum prolactin, serum and urinary cortisol and state and trait anxiety scores during the treatment cycle of women undergoing IVF (stimulated or unstimulated). The scores were compared with a control group of women undergoing similar gynecological surgery unrelated to IVF. In the stimulated IVF group, state anxiety increased significantly during the treatment. During the treatment, scores on state anxiety for this group were higher than the unstimulated IVF group. In addition, state anxiety scores in

the stimulated IVF group on the day that they injected human chorionic gonadotrophin (HCG) were significantly higher than the scores for the controls prior to surgery. No differences were found between and within the groups on trait anxiety. Information about the number of treatments the women underwent was not presented.

Median baseline serum prolactin concentration was significantly higher in the unstimulated IVF group and similar in the stimulated IVF group compared to that in the control group. In the stimulated IVF group, baseline concentrations were significantly lower than in the unstimulated IVF group. In the unstimulated group, prolactin concentration was significantly lower in the early follicular phase and increased during the phase the dominant follicle reached 15 mm (preoperative), whereas in the stimulated IVF group the concentration increased in both phases. During the preoperative phase, the prolactin concentration in the stimulated IVF group was significantly higher than in the control and unstimulated IVF group. Concerning serum cortisol concentrations, no differences were found between the control group and the unstimulated IVF group. For both groups, median concentration did not increase significantly during the treatment. In the stimulated group, median baseline concentration was significantly lower than in the unstimulated IVF group and increased during the treatment. There was uncertainty whether the rise in serum cortisol was solely oestrogen-mediated, or if it should be considered as a stress reaction.

In the study of Boivin and Takefman (1996), in which 20 women completed a daily symptom checklist for one complete menstrual cycle and one complete IVF cycle, it was found that IVF-women reported more optimism and physical discomfort than during a no-treatment menstrual cycle. They also felt more tired during IVF than during the no-treatment menstrual cycle.

## 5. Reactions following an unsuccessful IVF

For many couples, IVF is the last possibility to get their 'own' child. When the IVF-treatments are not successful, the couple has to face their infertility. Like the influence of the different stages of the IVF-procedure on psychological functioning, the failure of the treatment can also influence the psychosocial functioning of the man and the woman negatively.

After an unsuccessful IVF-treatment, couples may experience severe tension. Disappointment because of an IVF-failure is common (Leiblum et al., 1987). Other frequently occurring reactions to unsuccessful IVF are sadness, anger and depression, which are more pronounced in women than in men (Leiblum et

al., 1987; Baram et al., 1988). In a retrospective study, Baram et al. (1988) investigated 86 couples who completed IVF and did not become pregnant. Results showed that sadness was the most common feeling experienced after an unsuccessful IVF. Feelings of helplessness, loss and guilt were also common and were more pronounced in women than in men. Couples may feel cheated; after having endured a stressful IVF-treatment they have nothing in return. In addition, results revealed that no less than 66% of the women and 40% of the men reported depression following IVF failure. Depression was most acute immediately after IVF failure and decreased in severity over time for both men and women. One-third of the respondents were still depressed 18 months after the IVF treatment, with women reporting higher depression levels than men.

In a study of Leiblum et al. (1987), 59 couples who completed at least one IVF cycle were asked to complete pre- and post-IVF questionnaires. Women's reactions to an unsuccessful IVF were feelings of sadness and satisfaction at having attempted IVF. Also, among both men and women, ratings of anger and depression were significantly higher and ratings of vigor were significantly lower after unsuccessful IVF, in comparison with pre-IVF ratings. In addition, women in this study scored higher on depression and reported more feelings of guilt, anger and sadness after an unsuccessful IVF than did men. Women with biological or adopted children reported fewer feelings of anger and depression and higher vigor scores following unsuccessful IVF than women without children.

Hynes et al. (1992) examined 100 women progressing through an IVF treatment on psychological well-being at the beginning and end of a failed IVF. Seventy-three female controls also completed the measures on two points in time. As with the IVF-sample, two questionnaires were sent 4–6 weeks apart. Results revealed that IVF-women were more depressed and had lower levels of self-esteem than controls at time 2 but not at time 1. Also, IVF-women became more depressed over time and had lower self-esteem on the follow up. The controls did not change over time. Finally, IVF-women had lower scores on self-confidence than controls and levels of self-control for all women were higher at time 1 than time 2.

In the above studies, the number of IVF treatments couples underwent was not controlled for. It might be possible that couples react differently after their first failed IVF-treatment, compared to their future treatments. As Beaurepaire et al. (1994) noted, childlessness will be more current when after repeated IVF-procedures no pregnancy occurs, making women more vulnerable to developing clinically elevated depression.

Newton et al. (1990) assessed the psychological impact of failure after a first IVF-treatment in 213

women and 184 men, in comparison with the pre-IVF status. Results showed that women without children reported significantly greater anxiety after failure than women with children. Women with children showed little change in anxiety level after the failed IVF. In contrast, men reported a significant increase in anxiety after an unsuccessful IVF, regardless of whether they had children or not. For both men and women, depressive symptomatology increased significantly in the weeks after the unsuccessful IVF. Women had higher levels of depression than men. Although the mean scores of depression were in the normal range, 18% of the women and 8% of the men experienced mild depression, while 7.5% of the women reported more serious difficulties, characteristic of moderate levels of depression.

In a study of Litt et al. (1992), 41 women who presented for their first IVF cycle were studied to identify characteristics that predict adaptation following an unsuccessful IVF-treatment. They were assessed prior to the IVF and two weeks after the notice of the outcome of the treatment. Variables that predicted a poor adaptational outcome were pre-IVF distress, feelings of loss of control, attributing IVF-failure to oneself and escape as coping strategy. On the other hand, attributing infertility to oneself and dispositional optimism were protective of distress following an IVF failure and served as cognitive buffers against later distress. Situational optimism (estimated chances for success) was no predictor for post-IVF distress.

Slade et al. (1997) found that six months after completing the treatment, couples who completed three IVF cycles unsuccessfully were emotionally more distressed and showed poorer marital and sexual adjustment than the couples who achieved a successful pregnancy.

Women who were assessed before and after their first IVF-treatment showed an increase in depression and an improvement in the quality of their relationships after an unsuccessful IVF (Visser et al., 1994).

Researchers tend to describe the reactions following an unsuccessful IVF within the context of stressful aspects of IVF. However, reactions on a failed IVF-treatment can not solely be regarded as an effect of undergoing IVF. These reactions are the result of a complex interaction between reactions of undergoing the stressful aspects of IVF and the effect of experiencing infertility and, when IVF fails, again being confronted with childlessness. The differences between pre- and post-IVF measures are not only the result of the stressfulness of IVF and a negative outcome. The relatively low scores on pre-IVF measures may also be the result of the previously described self-selection effect (Callan and Hennessey, 1988; Edelmann et al., 1994) or the unrealistically high expectations of success on the treatment with which women start an IVF treat-



ment (Baram et al., 1988; Collins et al., 1992; Beaurepaire et al., 1994) and which may function as a strategy to cope with the tension and anxiety of an IVF-procedure (Shaw et al., 1988).

In a study of Domar et al. (1992a), the prevalence, severity and predictability in depression was determined in infertile women ( $n = 338$ ) compared with a control sample of healthy women ( $n = 39$ ). They found that the infertile women had significantly higher scores on depression than the control women. In infertile women, the prevalence of depressive symptoms was twice that of normal controls. The authors concluded that depression is a very common and significant problem in the infertile population and that it is the infertility per se and not the treatment that is associated with depression.

In this study, a nonlinear relationship was found between duration of infertility and depression. The third year of trying to conceive was associated with the highest depression scores. Depression scores peaked during the third year and then slowly fell to levels in the normal range after the sixth year.

## 6. Reactions following a successful IVF

### 6.1. The experience of pregnancy

When, after years of infertility and infertility treatments, a couple finally achieves a pregnancy, one might expect that they will experience more psychological problems during the pregnancy than couples who did not experience fertility problems. The previously infertile couple now finally gets what it fought for for such a long time. Anxiety to lose it may accompany the pregnancy period. Several studies addressed this issue.

In a study of Reading et al. (1989b), women who had conceived by IVF or gamete intrafallopian transfer (GIFT) did not differ significantly from women attending for genetic counselling in terms of state and trait anxiety. However, both groups scored higher on the standard measure of anxiety than normal primiparae, suggesting that increased anxiety may be a general characteristic of high risk pregnancies and is not unique to IVF groups (McMahon et al., 1995). They further demonstrated that in pregnant IVF-women, subjective ratings of anxiety and negative feelings toward the pregnancy decreased while attachment toward the foetus increased when seeing the foetal heartbeat through a reassuring ultrasound examination. However, although these investigators compared the IVF-women with a comparison group on the standard measures of anxiety, no comparison group was used concerning the effect of an ultrasound examination. The positive effects of reassuring feedback of the

foetus by ultrasound examination might be found in any female pregnant group.

In a review of psychosocial outcomes for parents and children after IVF, inconsistent support was found for heightened anxiety levels during pregnancy amongst women conceiving by IVF (McMahon et al., 1995). Reviewing these studies raised a number of methodological issues, like the use of small sample sizes and the limited sensitivity of global anxiety measures in the IVF-context. To provide more clinically meaningful information on how IVF couples experience pregnancy, these researchers compared 70 IVF parents with 63 matched controls at 30 weeks of pregnancy for their levels of anxiety and the quality of their attachment to the foetus and developed and incorporated a range of specific questions regarding concerns about pregnancy (McMahon et al., 1997). They concluded that the experience of pregnancy after infertility and IVF is stressful for most women. If no account was taken for the number of treatment cycles, results revealed that both IVF mothers and IVF fathers did not significantly differ from the control mothers and fathers on state and trait (global) anxiety, although both showed a tendency to differ. However, if the number of treatment cycles was taken into account, it appeared that IVF mothers who underwent two cycles differed significantly on state anxiety compared with the control mothers. No significant differences were found for the other subgroups or for the fathers.

Concerning specific pregnancy related anxiety in the mothers, IVF mothers significantly differed from the control mothers concerning their anxiety about the well-being of their unborn babies and about damage to the babies during childbirth. After comparing the treatment cycles, results showed that both IVF mothers who had undergone two treatment cycles and IVF mothers who had undergone three or more treatment cycles significantly differed on specific anxiety from the control group. No differences were found between the one-cycle group and the control group. However, the one-cycle IVF group scored significantly higher than the other groups on the measure of suppression of anxiety, suggesting they may be adopting a defensive coping style during pregnancy (McMahon et al., 1997). No differences were found between the IVF parents and control parents on foetal attachment.

van Balen et al. (1996) compared the experience of pregnancy and delivery among IVF patients, other formerly infertile parents (pregnancy without IVF) and fertile parents. Results suggested that IVF-parents and infertile parents who conceived without IVF, experienced more distress during pregnancy than normal fertile parents. IVF-fathers experienced the pregnancy as more exceptional and enjoyed it more than the fathers in the other groups. IVF-mothers and other formerly

infertile mothers experienced the delivery as more exceptional.

### 6.2. *The quality of parenting*

Several studies assessed the parent–child relation after in vitro fertilization (van Balen, 1995; Golombok et al., 1995; McMahon et al., 1995; Colpin, 1996).

Golombok et al. (1995) examined, among other things, the quality of the parent–child relationship in families with children conceived by IVF or donor insemination (DI). These families were compared with two control groups: a group of families with a naturally conceived child and a group of adoptive families. Significant differences between groups were found for age of the child, for age of the mother and for social class. However, because these three demographic measures were not significantly related with the measures of quality of parenting, these variables were not entered in the analyses as covariates.

We will here limit ourselves to describe the results concerning the IVF group and the families with a naturally conceived child. Contrast analyses showed that mothers with a child conceived by IVF expressed greater warmth toward their child and showed greater emotional involvement than mothers with a naturally conceived child. Mothers and fathers of children conceived by IVF showed greater interaction with their children than mothers and fathers of naturally conceived children. Results further indicated a greater incidence of marital difficulties and higher levels of anxiety and depression among parents with a naturally conceived child. The former group also reported significantly greater levels of distress than parents with a child conceived by IVF. However, it has been suggested that the exclusive reliance on self-report measures raises the possibility of a bias to positive self-reporting in the IVF group (McMahon et al., 1995).

McMahon et al. (1995) reviewed several other studies concerning the parent–child outcomes after IVF (Halasz et al., 1993; Raoul-Duval et al., 1993; Weaver et al., 1993). They concluded that these studies taken together provide no evidence that IVF families experience more parenting difficulties. However, because of, among other things, methodological problems and sample biases, the interpretation of the results is limited.

van Balen (1995) too failed to find evidence for parenting difficulties in IVF-families. In his study, parents with prolonged infertility who had a child through IVF and parents with prolonged infertility who had a child without IVF were measured with respect to parent–child relationship. The control group consisted of normally fertile parents. Significant age differences were found between the groups. Results showed that IVF-mothers and initial infertile mothers scored signifi-

cantly higher on emotional involvement and could handle their child better than the normally fertile mothers, even after controlling for differences in mother's age and gender of the child. No significant differences were found between the fathers. Again, because results are based on self-report, a possibility exists of a bias to positive self-reporting in the IVF-families.

Colpin (1996) compared 31 families with children conceived by IVF with 26 families with a naturally conceived child. After controlling for background variables, like education and age (significant higher for the IVF group), no significant differences were found between the two groups on behavior of the child or behavior of the mother in the attachment relationship or in the mother's or father's attitudes and emotions concerning the child's upbringing.

### 7. *Coping with in vitro fertilization*

The coping strategy most frequently used by couples when entering an IVF treatment program is taking direct action (Edelmann et al., 1994) and problem focused coping (Hearn et al., 1987). This may not be surprising, if one considers that undergoing an infertility treatment may be a problem focused strategy preeminently to deal with the fertility problems (Eugster and Vingerhoets, 1996).

Men and women tend to cope rather differently with infertility and IVF-treatment. In the study of Newton et al. (1990), women reported more open expression of feelings and greater involvement in social and/or recreational activities which are, according to the authors, congruent with suggestions that women are more likely than men to seek emotional and social support. For men, their greater orientation towards achievement is supposed to be consistent with the suggestion that men cope with infertility by greater involvement in work-related activities.

According to the cognitive model of coping of Lazarus and Folkman (1984), active problem focused strategies are more adaptive in controllable situations, while avoidant emotion focused strategies are more adaptive in uncontrollable situations. Entering and undergoing an IVF program includes elements of both controllable and uncontrollable events; couples can determine themselves whether they will undergo the treatment, but they have little control over its outcome (Edelmann et al., 1994). Some support for this model came from the study by Reading et al. (1989a), who found that women who at the beginning of the treatment believed that they had opportunities for control, showed lower scores on psychological measures following an IVF treatment than women who felt out of control.

Hynes et al. (1992), however, found opposite results. In their study, the use of problem focused coping to deal with a failed IVF, mainly cognitive strategies, was associated with high levels of well-being after a failed IVF. On the other hand, the use of avoidance coping was associated with low levels of psychological well-being. The authors suggested that using cognitive strategies may be adaptive, irrespective of the controllability of the situation, while with behavioural strategies, the controllability of the event is important.

In a retrospective study of Baram et al. (1988), couples were asked with whom they talked about infertility and IVF. For both partners, the spouse was their primary source of support, although close family members were also important sources. The researchers concluded that it is important that couples undergoing an IVF-treatment have the opportunity to express their feelings and concerns about the treatment. However, other coping mechanisms were not measured in this study.

Although weak, evidence has been found that women who sought social support to cope with a failure after an IVF attempt, had higher levels of depression after the failed IVF (Hynes et al., 1992).

#### **8. The effect of psychosocial factors on the treatment outcome after IVF**

After three IVF-attempts, about 60% of the couples have not achieved a pregnancy. Besides bio-medical factors, psychosocial factors seem to play a role in infertility. Garssen et al. (1989) reviewed the literature on the role of psychological factors in infertility of the period 1965–1986. The only consistent finding was that the anxiety level of infertile women was higher than of fertile women. Because most of the reviewed studies lacked a sound methodological basis, it was hard to conclude whether the increased anxiety should be considered as a reaction to infertility or as a causal factor. However, in a prospective study by Demyttenaere et al. (1988) it has been demonstrated that a relatively high trait anxiety level of the women is predictive for a lower chance of conception in normal, spontaneous cycles. Also, stress reduction through relaxation response exercises reportedly increases the probability of a pregnancy in women with mainly unexplained infertility (Domar et al., 1990). However, in the latter study, the majority of the participants had a diagnosis of unexplained infertility. The cumulative pregnancy-chance with an untreated group with unexplained infertility is 34% after six months, 74% after two years and after five years 87% (Garssen et al., 1989). There is therefore uncertainty whether the relaxation response exercises were the causal factor of increased pregnancy rates. In an attempt to replicate their pre-

vious findings, Domar et al. (1992b) studied women with different infertility diagnoses. Within 6 months after completing a behavioral treatment program, 32% of the women conceived. However, like in their previous study (Domar et al., 1990), the authors failed to compare the conception rate with a control group, thereby limiting conclusions concerning changes in conception rate through a behavioral treatment program.

Recent research results suggest that psychosocial factors may, at least partly, influence the outcome of an IVF-treatment. In three prospective studies (Demyttenaere et al., 1992; Thiering et al., 1993; Demyttenaere et al., 1994), ineffective coping strategies, anxiety and/or depression were associated with a lower pregnancy rate after an IVF-procedure.

In 40 women undergoing an IVF-treatment, Demyttenaere et al. (1992) studied the effect of coping style, depression and psychoendocrinological variables on the treatment outcome after IVF. They found that a combination of a high Zung depression score, high active coping (trying over and over again, even when it no longer makes sense to do so), high avoidance and a high expression of emotion was associated with a lower pregnancy rate. In addition, high anticipatory state anxiety levels in the early follicular phase or before oocyte retrieval, coupled with high anticipatory cortisol levels, were associated with a lower probability of conception during the IVF-treatment. Prolactin concentrations failed to predict the outcome of IVF, except in the early follicular phase, when high prolactin concentrations were associated with a negative treatment outcome. Demyttenaere et al. (1994) divided the group into two subgroups of 17 women with completely normal menstrual cycles and 23 women with subtle disturbances of their menstrual cycle. Results revealed that women with subtle cycle disturbances had lower pregnancy rates in IVF than women with normal cycles. Trait anxiety levels and prolactin concentrations were higher in women with subtle cycle disturbances. The state anxiety level in the early follicular phase, which has been shown to be associated with lower pregnancy rates in IVF (Demyttenaere et al., 1992), was higher in women with cycle disturbances.

In a prospective sample of 330 women, Thiering et al. (1993) studied the association between mood state and successful outcome among women undergoing IVF. Psychological measures were taken before commencement or the first day of the next treatment, whereas outcome measures (pregnant or not) were obtained up to 12 months after the beginning of the study. Results showed that amongst repeated cycle patients ( $n = 217$ ), depression measured at the start of their next treatment cycle was significantly associated with the treatment outcome. During the 1 year follow up, more of the nondepressed than of the depressed

women became pregnant. This association was not found amongst the first time participants ( $n = 113$ ). The authors hypothesized that the less predictive value of the depression scores of first cycle patients reflect their generally high expectations prior to commencing the treatment that they will be able to resolve their fertility problem through the IVF-treatment. This might also explain the significantly higher scores for veterans on depression, compared with the first cycle women. The authors emphasized that for a true reflection of mood states and their possible association with treatment outcome, the timing of psychological assessment of IVF-patients is critical.

Because outcome measures were obtained up to 12 months after the beginning of the study, the association between depression and outcome was assessed after having controlled for the number of IVF cycles prior to and during the 12-months follow up period. Results indicated that in the first 5–6 cycles, depressed veterans had a lower pregnancy rate than the nondepressed veterans. Beyond cycle 6, there appeared to be no differences in pregnancy rate between the depressed and nondepressed women.

Boivin and Takefman (1995) studied distress prospectively during IVF and its possible relationship to IVF-outcome. Their results showed that women who did not become pregnant ( $n = 23$ ) with IVF reported more distress during the treatment than women who became pregnant ( $n = 17$ ). In addition, compared to the pregnant group, the nonpregnant group had a poorer biological response to IVF in terms of E2 levels, oocytes retrieved and embryos transferred. These biological variables were also found to be related to distress during treatment. Boivin and Takefman (1995) had two possible explanations for their findings. First, they hypothesized that distress comprises patients' biological response to the different aspects of the IVF-treatment, which in turn leads to a poorer pregnancy rate. Their alternative explanation was the 'negative feedback' hypothesis, according to which negative feedback about the biological progress during the IVF-treatment may increase distress during the treatment.

Some contradictory results come from the study of Merari et al. (1992). In this prospective study, before the onset of the hormonal treatment, during the phase of the embryo transfer and the phase of the pregnancy test, no significant differences were found in depression, trait and state anxiety between the women who conceived ( $n = 23$ ) and the women who did not conceive ( $n = 62$ ). However, during the phase of the oocyte retrieval, women who conceived scored higher on state anxiety than the women who did not conceive. This finding is opposite to what Demyttenaere et al. (1992) have found, namely that a high state anxiety level in the early follicular phase and before oocyte

retrieval is associated with lower pregnancy rates after IVF-treatment. Merari et al. (1992) hypothesized that the women who did not conceive used repression as a coping strategy, which resulted in low anxiety test scores. Because repression is generally considered as maladaptive coping, tending to repress one's emotions is a less effective way to cope with the distress caused by an IVF-treatment. However, in this study no coping strategies were measured to support this hypothesis.

Hormonal levels (cortisol and prolactin) were correlated with behavioral parameters (state anxiety and depression) only during the phase of the pregnancy test. In this phase, in the women who conceived, a significant negative correlation was found between hormones and the psychological measures, whereas no relationship was found between these parameters in the women who did not conceive. Because both hormones showed a highly significant rise during the phase of the pregnancy test in both groups, the researchers hypothesized the involvement of a mediating factor; an additional factor active in the central nervous system in a state of anxiety had a mediating role between the mental state and hormone secretion.

In a second study (Merari et al., 1996) with the same 113 childless women, data collected prior to the initiation of the IVF-treatment were used to predict the outcome after IVF. A stepwise logistic regression model was employed to identify parameters that could predict the outcome after IVF. The results showed that the chances for success were inversely related to age and the level of the couples' cohesion. A positive outcome after IVF was more likely to occur among women who: (a) were defined as traditional (religious observance), (b) initiated adoption procedures, (c) had a higher emotional involvement and (d) had a moderate rise in cortisol level.

The findings that defining oneself traditional with respect to religion and initiating adoption were predictors for the outcome after IVF, were interpreted by the investigators in the context of active coping. No direct measures of coping were used in this study. Also, initiating adoption as a predictor for the outcome after IVF could be interpreted in the context of cumulative pregnancy chance for women with unexplained infertility. In this study, female infertility was due to either an unknown cause or a mechanical cause. With unexplained infertility, the chance of pregnancy is not impossible and even relatively high (Garssen et al., 1989). Because of a high cumulative pregnancy probability, it is possible that in a considerable part of couples with unexplained infertility a pregnancy occurs when they are in the middle of an adoption procedure. This may erroneously lead to the conclusion of a causal relation between adoption and pregnancy.

Several studies failed to find evidence for a relationship between psychosocial factors and treatment out-

come after IVF (Visser et al., 1994; Harlow et al., 1996; Slade et al., 1997). However, Visser et al. (1994) noted that the number of observations in their study was relatively small, which also limited correcting the analyses for the influence of various medical factors on the chance of pregnancy after IVF.

In the study of Harlow et al. (1996) with women undergoing IVF, trait anxiety scores at median baseline (at initial consultation) and during the phase the dominant follicle reached 15 mm (preoperative) were higher in IVF women who did not become pregnant, compared with the IVF women who became pregnant. During the early follicular phase and preoperative phase, state anxiety scores were higher in unsuccessful IVF women, compared with the IVF women who became pregnant. For both state and trait anxiety, the differences were not significant. However, these authors also noted that their numbers were too small to be statistically conclusive.

Slade et al. (1997) found no significant difference in emotional state or relationship factors at the initiation of the IVF-treatment between couples who completed three IVF cycle unsuccessfully and the couples who achieved a successful pregnancy. However, these results have to be viewed cautiously. During the longitudinal study, the initial sample decreased from 144 couples to 42 pregnant and 14 not pregnant couples. Couples were omitted for several reasons, mainly because they did not complete all available treatments. No information was available why these couples did withdraw from the program. This information might be highly important in predicting psychological functioning during and after a failed IVF, or the outcome of IVF.

### 9. The effect of psychological interventions on conception rates

Domar (1997) stated that if stress may contribute to infertility, then it may be hypothesized that stress reduction will improve conception rates. She indeed found support for the hypothesis. Relaxation training for women with unexplained infertility (Rodriguez et al., 1983) or women who were to undergo an IVF (Farrar et al., 1990) resulted in higher conception rates in the experimental groups than in the control subjects. Also, drug intervention to reduce anxiety in women with unexplained infertility led to higher conception rates, compared with control subjects who received a placebo (Sharma and Sharma, 1992). The results of the studies of Rodriguez et al. (1983) and Sharma and Sharma (1992) can not be explained by a cumulative pregnancy rate in women with unexplained infertility, because the control groups also consisted of infertile women in which the cause of infertility could not be established.

In an attempt to replicate their own previous findings (Domar et al., 1990), Domar et al. (1992b) assessed 52 women with infertility problems who attended the Behavioral Medicine Program for Infertility, to measure the effect of a clinical behavioral medicine treatment program for infertile women on psychological symptoms and conception rates. While in their previous study women with mainly unexplained infertility were assessed, in this replication study women with different infertility diagnoses (like endometriosis and a male factor) participated.

The women attended a 10-week group behavioral treatment program which included, among other things, relaxation response training, stress management and nutritional education. Before entering and after the treatment program, the women completed a battery of psychological tests, measuring mood, anxiety and anger. Results showed that, like in their previous study, the behavioral treatment program reduced psychological symptoms of depression, anxiety and anger. Also, within 6 months after completing the program, 32% of the women conceived. However, because the authors failed to compare the decrease in psychological symptoms and the conception rate with a control group, any definitive conclusions concerning changes in levels of psychological symptoms and conception rate are not possible. However, according to Domar (1997), spontaneous reductions in psychological symptoms in women undergoing infertility treatment are rare, suggesting that it is likely that the improvements in psychological symptoms found in their studies (Domar et al., 1990, 1992b) were indeed related to the behavioral treatment.

### 10. Conclusion

Results of several studies strongly suggest that it is important to assess respondents' psychological reactions during different phases of the IVF procedure. There is consensus concerning couples' general psychological well-being when entering an IVF treatment program. Couples appear to be, in general, psychologically well adjusted. However, more specifically, some researchers have found that women, entering an IVF program, score above the norm on measures of anxiety, while others did not find any significant differences with normative data.

There is also consensus about the phases which are experienced as most stressful, namely waiting for the outcome of the treatment and an unsuccessful IVF-treatment.

Contradictory results have been found concerning anxiety during IVF. Although both men and women appear to experience anxiety during the treatment, with women more than men, some researchers have

found that state anxiety decreases during the treatment (Connolly et al., 1993), while others have found an increase in state anxiety during the treatment (Harlow et al., 1996). A closer look at the studies reveals that measures were taken at different occasions during the treatment. While Connolly et al. (1993) measured couples twice before the IVF and just after the treatment, Harlow et al. (1996) measured during the treatment. Again, the importance of the time point when to measure psychological factors is underlined.

Concerning the effect of psychosocial factors on the treatment outcome after IVF, results are contradictory. Several studies are characterized by methodological flaws, for instance, small sample sizes or a high drop out rate. However, the role of stress in infertility and infertility treatment outcome remains intriguing. In the few studies concerning the effect of psychological interventions on conception rates, it has been found that stress reduction by relaxation training or stress management reduces psychological symptoms and at the same time increases the conception rates, suggesting that stress indeed may contribute to infertility. As Mazure and Greenfield (1989) noted, although an underlying psychological flaw does not cause infertility, the reaction of stress to infertility may influence physiological outcome in both men and women.

In order to find out whether psychological factors can predict infertility and outcome after an infertility treatment, it is necessary to study couples prospectively over a longer time period. In addition, for a methodologically well-structured design, sample sizes have to be calculated on the basis of mean pregnancy chances when undergoing an infertility treatment. In addition, psychobiological variables, indicating whether distress is experienced, have to be measured. Only then can be established whether psychological factors can influence treatment outcome.

It is generally recognized that both psychosocial and psychobiological research within the context of reproductive technologies are important. Both research approaches help us to understand how couples react to the infertility treatment. Research within this context can result in more knowledge about the influence of psychosocial and psychobiological factors on the treatment outcome.

However one has to bear in mind that, in order to draw any reliable conclusion, one can not limit oneself to retrospective studies only. If one wants to make any firm statements about which variables play an important role in reproductive technologies, one has to study couples prospectively. Even then it will be difficult to separate reactions from undergoing an infertility treatment to reactions which result from experiencing infertility per se, because they are intertwined in such a complex way. Most importantly is that more knowledge enables us to help couples experiencing the rather

stressful infertility treatments to resolve their fertility problems.

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